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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
MYERS, CARLA J

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,066	ANAND ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6/2/01* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. Applicant's election with traverse of group I in the response of December 20, 2002 is acknowledged. The traversal is on the ground(s) that the claims cover the detection of one or more polymorphisms and thereby the claims of groups II and III should be examined together with the claims of group I. While none of the previously presented claims specifically required the detection of 2 or 3 of the stated polymorphisms, it is acknowledged that newly added claim 13 does require the detection of all 3 polymorphisms. Since this constitutes a limited set of polymorphisms, each of these polymorphisms will be examined herein. Accordingly, groups I, II and III have been rejoined. The remaining groups are withdrawn as being drawn to a non-elected invention. This aspect of the restriction requirement is still deemed proper and is therefore made FINAL.

2. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Definitions: [from UTILITY GUIDELINES TRAINING MATERIALS; repeated from

http://www.uspto.gov/web/menu/utility.pdf]

"Credible Utility" - Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, Office personnel must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic

underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A *credible* utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the *specific* and *substantial* tests (see below).

"Specific Utility" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a *specific* or *substantial* utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. ' 101. This analysis should, or course, be tempered by consideration of the context and nature of the invention. For example, it a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial *asserted* utility would be considered to be met.

"Well established utility" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this is the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight; any carbon containing molecule would have a "well established utility" as a fuel since it can be burned;

any protein would have well established utility as a protein supplement for animal food. This is not the intention of the statute.

See also the MPEP at 2107 - 2107.02.

3. Claims 1-10 and 13 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, substantial, specific or well-established utility.

The claims are drawn to methods for diagnosing a single nucleotide polymorphism in the PDK2 gene and to nucleic acids comprising a polymorphism at position 288, 1281 or 1357 of the PDK2 gene. The claimed nucleic acids are not supported by either a specific and substantial asserted utility or a well-established utility. The specification fails to provide objective evidence of any activity for the claimed nucleic acids containing polymorphisms. The specification states that the claimed nucleic acids can be used in diagnostic or therapeutic assays. In particular, the specification (page 3) indicates that the presence of one of said polymorphisms in the PDK2 gene can be used to assist in drug selection processes and in identifying patients suited for therapy. The specification also suggests that the PDK2 gene has a regulatory role in the control of NDDM and obesity (pages 16-17). However, the specification has not established that the stated polymorphisms in the human PDK2 gene are associated with any disease or condition, particularly with the conditions of NDDM and obesity. The specification provides information regarding the activity of PDK2 in rats, but does not provide any information regarding the activity of PDK2 in humans. There is no information provided in the specification which would indicate that the disclosed polymorphisms are associated with an alteration in the expression or activity of PDK2. The specification (page 3) further suggests that the 288, 1281 and 1357 polymorphisms

can be used to map the human genome. However, such a utility is general because it is a property of all polymorphisms and thereby is not considered to be a specific utility. The specification (page 3) also states that the polymorphisms can be used to elucidate genetic components of a disease. However, such a utility is not considered to be substantial because it essentially involves performing research in order to find a utility for the polymorphisms. As stated in Brenner v. Manson, 383 U.S. 519 535-536, 148 USPQ 689, 696 (1966) " a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion". Support for an asserted utility that is specific and substantial would require, for example, a showing of a particular function for the PDK2 polymorphisms, or a showing of a clear correlation between the disclosed polymorphisms and the occurrence of disease or an alteration in drug metabolism or response to drug treatment. Merely identifying and studying the properties of the polymorphisms or performing linkage analysis assays to determine a correlation between the polymorphisms and disease or drug responsiveness does not constitute a "real world" context of use. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid compounds such that another non-asserted utility would be well established for the compounds. Accordingly, the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

4. Claims 1-10 and 13 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Furthermore, it is noted that the specification has not established a correlation between the stated polymorphisms and any particular disease or response to therapy. Extensive experimentation would be required to establish that a particular polymorphism is associated with a disease and the showing that a polymorphism is associated with one disease would not be sufficient to establish that the same polymorphism is associated with all diseases mediated by PDK2. Additionally, the specification (page 3) teaches that a "PDK2" drug is intended to encompass any drug that changes the level of PDK2 or changes the activity of PDK2. The specification also cites 2 references as teaching PDK inhibitors. However, the specification has not taught any therapeutics which alter PDK2 activity and which could be used to treat individuals carrying the stated PDK2 polymorphisms. The specification does not provide any information regarding how the presence of the PDK2 polymorphisms alter response to therapy and thereby has not enabled methods in which the presence of a PDK2 polymorphism can be used to predict a clinical response to a therapeutic compound or to aid in determining the dose of a therapeutic compound. No specific guidance has been provided in the specification for performing such methods. It is also highly unpredictable as to how the presence of the polymorphism alters PDK2

activity or expression and as to how this would affect an individual's response to therapy. Accordingly, the specification has not enabled the invention as it is claimed.

5. Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 6 is drawn to a nucleic acid comprising a sequence sharing any level of sequence complementarity with nucleic acids having a polymorphism at position 288, 1281 or 1357 of EMBL Accession No. L42451, antisense sequences thereto and fragments thereof of at least 20 bases comprising at least one polymorphism. The broadest reasonable interpretation of the claim indicates that the claims are inclusive of sequences which share any level of sequence complementarity with PDK2 nucleic acids and which may have any function. The claim also includes novel nucleic acids which are defined only in terms of containing 20 nucleotides of the PDK2 gene and in which the flanking nucleotides are not defined and the functional activity of the nucleic acid is not defined. Because the nucleic acids are defined in terms of comprising 20 mer fragments of the PDK2 gene, the claims also include genomic sequences and splice variants of PDK2. Additionally, because the fragments do not recite a particular polymorphism, the claim also includes polymorphisms in addition to those at position 288, 1281 and 1357. However, the specification and art teach only a single PDK2 gene, i.e., that which has the sequence of GenBank/EMBL Accession No L42451. The specification also teaches only the 3 polymorphisms

at positions 288, 1281 and 1357. The specification does disclose any additional allelic variants, any genomic sequences, any splice variants or any additional non-PDK2 genes that contain 20 mer fragments of the sequence of GenBank/EMBL Accession No L42451. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of specifies have been described by their complete structure. In the instant case, only 1 member of the broadly claimed genus have been defined by their structure, i.e. nucleic acids having the sequence of GenBank/EMBL Accession No L42451. It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g. restriction map, chromosomal map position, biological activity of an encoded protein product, etc.). In the instant case, no such identifying characteristics have been provided for any of the nucleic acids. While at the time of filing applicants were in possession of nucleic acids having the sequence of

GenBank/EMBL Accession No L42451 and nucleic acids which differ from the sequence of GenBank/EMBL Accession No L42451 in that they contain a polymorphism at position 288, 1281 or 1357, the specification provides no information regarding genomic PDK2 sequences, additional polymorphisms, or variant nucleic acids of PDK2 or non-PDK2 genes sharing any level of sequence complementarity with nucleic acids of GenBank/EMBL Accession No L42451 or containing 20 mer fragments of the nucleic acids of GenBank/EMBL Accession No L42451. Therefore, the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

6. Claims 1-10 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1-10 and 13 are indefinite and vague over the recitation of "EMBL ACCESSION NO: L42451" because it is not clear as to what is encompassed by this phrase. The sequences listed in EMBL/GENBANK are continuously updated and modified. For example, this particular accession number was created on November 30, 1995, and was first modified on February 8, 1997 and modified again on September 23, 1998 (see attached printout from the NCBI database) . Accordingly, there is no single, constant definition for the sequence presented as Accession No. L42451.

B. Claims 4 and 5 provide for the use of a method according to claims 1-3, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. It is unclear as to the relationship between the methods of claims 4 and 5 and the methods of claims 1-3. For example, it is unclear as to whether claim 4 is intended to be limited to a method of predicting a clinical response to a therapeutic compound, or a method for determining the therapeutic dose of a compound or a method for treating a PDK2- mediated disease or if claim 4 is intended to be limited to a method for diagnosing a single nucleotide polymorphism. In the former case, the claim does not set forth the method steps which achieve these uses. For example, the claims do not clarify how the step of determining the status of a human results in the prediction of a clinical response to a therapeutic compound.

C. Claim 6 is indefinite over the recitation of "at least one polymorphism" because it is unclear as to whether this refers to any polymorphism in the PDK2 gene or to one of the polymorphisms selected from the group consisting of the polymorphisms at positions 288, 1281 or 1357.

D. Claims 7-9 are indefinite over the recitation of "capable of detecting" because capability is a latent characteristic and the claims do not set forth the criteria by which to determine capability. That is, it is not clear whether the recited primers and probes have the potential to detect or do in fact detect the stated polymorphisms. This vague language does not clarify the

structure of the primer and probe and does not allow one of skill in the art to determine the meets and bounds of the claimed invention.

6. Claims 4 and 5 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

7. Claims 4 and 5 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiply dependent claim. See MPEP § 608.01(n).

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-8 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Gudi (cited in the IDS as reference "SR").

Gudi et al teach a nucleic acid comprising the PDK2 gene. This nucleic acid was deposited as GenBank/EMBL Accession No. L42451 (see page 28989, column 1). Gudi also teaches methods of sequencing the PDK2 gene. It is noted that claims 1, 2 and 13 are broadly drawn to

methods for diagnosing a single nucleotide polymorphism in the PDK2 gene. The claims recite a single step of determining the sequence of the PDK2 gene at positions 288, 1281 and/or 1357 of EMBL Accession No. L42451. The recitation in the preamble does not result in a manipulative difference in the method steps when compared to the prior art disclosure. Since the method steps recited in the claims (i.e., determining the sequence of the PDK2 gene at positions 288, 1281 and 1357) are the same as those set forth by Gudi, the methods of claims 1 and 2 are anticipated by the disclosure of Gudi. With respect to claims 4 and 5, the intended use of the method of sequencing the PDK2 gene does not distinguish the claimed method over that of Gudi. With respect to claim 6, the claims are inclusive of nucleic acids sharing any level of sequence complementarity with the stated sequence. The complementary and antisense sequences need not include the stated polymorphisms and the sequences may differ by any degree of complementarity from the PDK2 sequence. Additionally, the fragments need not include the polymorphism at position 288, 1281 or 1357. The fragments also include either a C or T at position 288, either a G or A at position 1281 and either a G or C at position 1357 and include full length PDK2 sequences. Accordingly, claim 6 reads on the wild-type PDK2 sequence disclosed by Gudi. With respect to claims 7 and 8, the recitations of primer and probe do not impart any specific length limitations and the claims include both allelic variants of the PDK2 polymorphisms. Accordingly, these claims also read on the wild-type PDK2 gene of Gudi.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gudi in view of the Stratagene Catalog (1988).

Gudi et al teach a nucleic acid comprising the PDK2 gene. This nucleic acid was deposited as GenBank/EMBL Accession No. L42451 (see page 28989, column 1). Gudi also teaches methods of sequencing the PDK2 gene. It is noted that the recitations in claims 7 and 8 of primer and probe do not impart any specific length limitations on the claimed nucleic acids. In addition, the claims include PDK2 nucleic acids comprising either a C or T at position 288, either a G or A at position 1281 and either a G or C at position 1357. Accordingly, the claims read on the wild-type PDK2 gene of Gudi. Gudi does not teach packaging these nucleic acids in a kit.

However, reagent kits for performing diagnostic methods were conventional in the field of molecular biology at the time the invention was made. Therefore, it would have been prima facie

obvious to one of ordinary skill in the art at the time the invention was made to have packaged the PDK2 nucleic acids of Gudi in a kit for the expected benefits of convenience and cost-effectiveness for practioners in the art wishing to further characterize the PDK2 gene, to analyze its expression or to synthesize PDK2 proteins.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)-308-1119. Papers related to this application may be faxed to Group 1634 via the PTO Fax Center using the fax number (703)-872-9306 or (703)-872-9307 (after final).

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers

March 13, 2003

Carla Myers

CARLA J. MYERS
PRIMARY EXAMINER